



# Middle East respiratory syndrome coronavirus in healthcare settings

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## Purpose of review

Attracting global attention, Middle East respiratory syndrome coronavirus (MERS-CoV) continues to cause sporadic cases and a potential risk of healthcare-associated infections. In this review, we highlight what is known about the risk of transmission within healthcare facilities and discuss interventions to halt its transmission within healthcare.

## Recent findings

MERS-CoV causes a wide range of infections from asymptomatic infections, mild or moderately symptomatic cases, to fatal disease. Two years after the initial reported case, MERS-CoV has caused limited disease outside the Arabian Peninsula with several cases in Europe, Asia, and the United States. Epidemiologically, these infections are linked to exposures from the region and their diagnosis outside is related to travel. Several reported clusters of disease report multiple transmissions of MERS-CoV within healthcare settings that have been attributed to poor compliance with the basic infection control measures. Factors contributing to the spread and control of MERS-CoV within healthcare settings have not been elucidated so far. Data suggest the overcrowding, late recognition of MERS-CoV cases, and inadequate infection control practices contribute significantly to the transmission.

## Summary

Understanding factors contributing to the spread and the dynamic of MERS-CoV transmission within healthcare settings would further enhance the control of the disease in and outside the healthcare setting.

## Keywords

coronavirus, healthcare facilities, Middle East respiratory syndrome coronavirus, prevention, transmission

## INTRODUCTION

There are six human Corona viruses (hCoV) known to cause human respiratory tract infections. These include HCoV-229E, HCoV-OC43, HCoV-NL63, HCoV-HKU1, Severe Acute Respiratory Syndrome Coronavirus, and the Middle East respiratory syndrome coronavirus (MERS-CoV) [1,2]. In 2012, MERS-CoV was identified from a patient who was admitted with progressive pneumonia in the Kingdom of Saudi Arabia [3]. Since then, a total of 952 cases have been reported with a case fatality rate of 43.4% [4]. The clinical presentation and the epidemiology of the disease were reviewed recently [5<sup>•</sup>,6<sup>•</sup>,7–10]. Importantly, MERS-CoV was described among healthcare workers and in healthcare settings leading to amplified transmission [11<sup>••</sup>–13<sup>••</sup>,14<sup>•</sup>,15]. In this review, we discuss available data regarding healthcare transmission of MERS-CoV and summarize known risk factors and key measures for the control of the disease within healthcare settings.

## Transmission of Middle East respiratory syndrome coronavirus within the healthcare facility

Since the initial description of MERS-CoV infection, the virus has caused outbreaks within healthcare facilities [11<sup>••</sup>–13<sup>••</sup>,14<sup>•</sup>,15], yet there remains a paucity of data to guide policy in many arenas. Since the initial description of the disease in June 2012 until 14 March 2015, a total of 952 MERS cases were reported in Saudi Arabia alone [4]. Of the total

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## KEY POINTS

- Factors contributing to the spread and control of MERS-CoV within healthcare settings have been poorly elucidated.
- Multiple transmissions of MERS-CoV within healthcare settings are attributed to poor compliance with the basic infection control measures.
- Proper infection control application would prevent the transmission of MERS-CoV within healthcare settings.

748 cases reported as of September 2014, approximately 27% were healthcare workers [16]. The transmissibility of the virus in healthcare settings depends on the case finding and the infection control measures in place. Hence, there are gaps in our knowledge. For example, transmission within the healthcare setting was recognized retrospectively in the outbreak described in Jordan [14<sup>15</sup>], later such transmission was documented among almost one-third of cases in the Al-Hasa outbreak [11<sup>12</sup>] and in Jeddah, Saudi Arabia [12<sup>13</sup>]. Two of 13 people (including 10 healthcare workers) were confirmed to have MERS CoV infection using rRT-PCR in the Jordanian outbreak in Zarqah [14<sup>15</sup>]. Based on the serologic studies, an attack rate of 10% was reported among exposed healthcare workers and 5% of family contacts [15]. Other studies have, however, not demonstrated transmission among healthcare providers including those reported from the United Kingdom, France, and Saudi Arabia [5<sup>17–19</sup>]. A group of healthcare workers from a single hospital of whom 48 had and 48 did not have contact with a MERS-CoV case revealed that MERS-CoV was not detected in any of those contacts by serologic testing [19]. A summary of the studies evaluating transmission of MERS-CoV among patients, healthcare workers, and others is shown in Table 1 [13<sup>14</sup>, 15–20, 21<sup>22</sup>, 23, 24].

### Factors contributing to inter- and intrahospital transmission of Middle East respiratory syndrome coronavirus

Several factors may contribute to the reported inter- and intrahospital transmission. First, similar to other respiratory tract infections, initial symptoms of MERS-CoV are not specific hampering the initial identification of these patients. Furthermore, the period of communicability of MERS-CoV, the duration of viral shedding, or characteristics that enhance viral shedding have not been defined. Although healthcare workers are advised to practice standard and droplet precautions when dealing with

any patient with an acute respiratory infection [25], compliance with respiratory etiquette and infection control practices remain a challenge. A study of 48 healthcare workers found that upper respiratory symptoms developed in 27% of those who cared for MERS-CoV positive cases compared with 33% of those who did not have contact with MERS-CoV patients [19]. Of the 48 with case-contact, 87.5% reported wearing a medical mask, and 33% reported wearing an N-95 mask [19]. Because individual healthcare workers may report wearing both forms of respiratory protection, the total percentage is more than 100% [19]. The study did not address the difference between those who had symptoms and those who did not have symptoms.

Still, in other healthcare settings, MERS-CoV transmission is described among healthcare workers and patients. In the 2013 Al-Hasa outbreak, 21 of 23 infections were considered healthcare acquired and associated with intrahospital transfer and likely inadequate infection control [11<sup>12</sup>]. Of more than 200 exposed healthcare workers, only two laboratory-confirmed cases were identified among them [11<sup>12</sup>]. Of note, this outbreak spanned over four hospitals and occurred early in the time line of the disease. Importantly, this outbreak occurred before the full spectrum of illness was appreciated and a search for healthcare workers in contact with cases was actively done [19]. The most recent outbreak in Jeddah (February–April 2014) involved 128 MERS-CoV patients in 14 hospitals, in which the infection was amplified in the healthcare setting [12<sup>13</sup>]. Subsequently, 109 of 112 (97.3%) of symptomatic nonhealthcare workers were thought not to be primary cases [13<sup>14</sup>]. In another setting, transmission of MERS-CoV was reported between two immunosuppressed patients in the United Kingdom, yet the exposures were not described [26].

In an attempt to define the risk of acquisition of MERS-CoV in various settings and more systematically, investigators in the Kingdom of Saudi Arabia reviewed data from over 2908 cases and found that 72 (2.5%) were considered related to nosocomial transmission [20]. To determine how commonly MERS-CoV was transmitted in among healthcare workers, they used nasopharyngeal swabs to screen 1695 healthcare workers who were in contact with cases between 1 October 2012 and 30 September 2013 [20]. Only 19 (1.1%) of these healthcare workers had evidence of MERS-CoV by PCR [20]. This attack rate is lower than that reported among family contacts of 3.6% (17 out of 462 of contacts) [20]. One study of 70 cases found a higher rate of transmission between 2012 and 2014 with eight (11%) healthcare-associated MERS-CoV infections [27] with the largest cluster being in the emergency

**Table 1.** Healthcare associated MERS-CoV outbreaks and clusters

Reference	Total number of cases/contacts	Number of HCWs (% of the total cases)	Respiratory symptoms (%)	N (%) MERS positive HCW	Method of testing	Fatality	Country
14	191 symptomatic cases	81 (42.4)	40 (21)	40 of 81 tested (50%)	PCR	NA	KSA
14	64 asymptomatic cases	NA	0 (0)	41 (64)	PCR	NA	KSA
15	124 contacts	89 (71)	0 (0)	6 (6.7)	Serology or PCR	Two of nine cases (22%)	Jordan
16	Two laboratory-confirmed and 11 probable cases	10 HCWs suspected	13 (100)	Two laboratory-confirmed	Serology	NA	Jordan
17 (June 2012 to 18 September 2014)	748 cases	NA	PCR	202 (27)	PCR	NA	KSA
18	64 contacts	56 (87.5)	13 (23)	0 of ted (0)	Serology	0	UK
19	123 contacts	110 (89.4)	NA	0 (0)	PCR	0	France
20	48 contacts	48 (100)	0	0 (0)	EIA	0	KSA
21	5065 contacts	1695 contacts (33)	0 (0)	19 (1.12)	PCR	0	KSA
22	520 contacts	4 (7.6)	4 (100)	4 (14)	PCR	0	KSA
23	NA	7		7 (100)	PCR	NA	KSA
24	255 cases	65 (25.5)	NA	39 (30.4)	PCR	NA	KSA
24	37 cases		NA	25 (67)	PCR	NA	UAE
25 (19 September 2014 to 24 March 2015)	200 cases	80 (40)	NA		PCR	NA	KSA

EIA, enzyme immunoassay; HCWs, healthcare workers; KSA, Kingdom of Saudi Arabia; MERS-CoV, Middle East respiratory syndrome coronavirus; NA, not available; PCR, polymerase chain reaction; UAE, United Arab Emirates; UK, United Kingdom.

department [27]. More recent studies have identified that the majority of healthcare workers who developed MERS-CoV infection were younger women, and were asymptomatic or mildly symptomatic [23]. Severe disease was described in 15% of healthcare workers and led to hospitalization, ICU admission, or death [23]. Most of the affected healthcare workers were nurses indicating the importance of prolonged, repeated, and close physical contact with MERS-CoV patients [15].

### **Proportion of healthcare-associated infection among Middle East respiratory syndrome coronavirus cases**

According to the WHO MERS-CoV Research Group, of 95 MERS-CoV cases 63.2% were healthcare associated and 13.7% were family contacts [28]. In a study of 70 cases from one hospital, at least 50% of the cases were acquired in the hospital setting [27]. In the 2014 Jeddah outbreak, there were 128 laboratory-confirmed cases in 14 hospitals between 17 February and 26 April 2014 [13<sup>22</sup>,23,29]. Of these cases, 33% were primary cases and more than 60% (including 39 healthcare workers) were acquired within healthcare facilities [23].

### **Factors contributing to intrahospital transmission**

Data are limited about the specific factors accounting for the transmission within healthcare facilities. Overcrowding, close proximity of patients to cases, delay in isolation of cases as in the Al-Hasa outbreak, and the use of aerosol generating and high-risk procedures were, however, thought to contribute to the transmission [11<sup>22</sup>]. Possible factors contributing to healthcare transmissions of MERS-CoV may include the following: super-spreader cases who shed virus extensively, prolonged viral shedding, and suboptimal infection control measures.

### **'Super-spreader' of Middle East respiratory syndrome coronavirus**

Super spreaders are individuals who spread disease to multiple individuals. The number of secondary transmissions of MERS-CoV from a single case is variable; however, in one study, one patient transmitted MERS-CoV infection to 10 other patients [27]. In the Al-Hasa outbreak, one patient with MERS-CoV transmitted the infection to seven other individuals [11<sup>22</sup>]. No further analysis of the frequency of transmission was delineated to characterize the frequency of the occurrence of secondary and tertiary transmission.

### **Prolonged viral shedding**

Prolonged viral shedding of patients and asymptomatic contacts is reported and poses potential important challenges for infection control [30]. MERS-CoV in two patients was detected for prolonged periods, up to 18 and 24 days, from the respiratory tract secretions using rRT-PCR [31,32]. Importantly, studies have identified MERS-CoV by rRT-PCR in asymptomatic family contacts, and healthcare workers [20]. In fact, MERS-CoV was detected in 30% of 'case' contacts 12 days after exposure [33]. During the 2014 Jeddah outbreak, an asymptomatic healthcare worker was shedding MERS-CoV for almost 6 weeks; from 24 April 2014 to 12 June 2014 [34].

### **Controlling nosocomial transmission**

The tenets of controlling transmission of respiratory viruses are well demonstrated with MERS-CoV infections. Public health authorities have provided varying recommendations regarding MERS-CoV infection control practices in healthcare settings. The WHO advocates contact and droplet precautions and the use of airborne isolation precautions during aerosol generating procedures. Whereas the United States and the European Centers for Disease Control and Prevention advocate the use of airborne isolation precautions for all patients in all settings [35–37]. All public health authorities advocate for aggressive surveillance to identify potential cases with the use of isolation when a case is suspected.

### **Application of infection control measures**

Basic infection prevention is important and includes the use of standard precautions and compliance with hand hygiene. Interhospital and intrahospital transmission of MERS-CoV infection is a risk and as found in the Al-Hasa outbreak could be aborted by early recognition of cases and the universal use of standard and droplet precautions when in contact with patients with respiratory symptoms [11<sup>22</sup>,27]. Airborne isolation should be specifically used in those patients requiring aerosol-generating procedures [36,37]. It is of paramount importance that patients be cohorted to avoid cross transmission between patients. Furthermore, healthcare workers may be a source of transmission. Asymptomatic healthcare workers shed MERS-CoV and could infect susceptible patients and coworkers should be evaluated carefully. Ideally, they should be furloughed until they are no longer shedding MERS-CoV as indicated by negative MERS-CoV tests. Repeated MERS-CoV testing is indicated every 3 days after initial positive screen until documentation of at least two negative tests.

## CONCLUSION

MERS-CoV is the newest of the respiratory viruses to emerge and be characterized by transmission in healthcare settings. Yet, the transmission of MERS-CoV within a healthcare facility remains poorly studied and an important issue to understand to implement control. While transmission has been documented in multiple outbreaks, the overall risk of transmission appears low. Infection control recommendations are based on knowledge from Severe Acute Respiratory Syndrome and other corona viruses and include standard precautions and droplet or airborne precautions. Further systematic collections of data in relation to outbreak control measures and factors leading to outbreak are needed to refine policies and procedures to combat the disease.

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## Conflicts of interest

There are no conflicts of interest.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

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